REMARKS

Claims 32-51 and 57-62 are pending in the application. Claims 52-56 have been canceled as directed to a non-elected invention. Claims 57-62 have been added. Support for the new claims can be found in the specification at, e.g., page 8, lines 8-11. These amendments add no new matter.

Claim 43

At page 2 of the Office Action, the Examiner stated that a correction from "BP1" to "VP1" in claim 43 is required. Applicants made this correction of claim 43 in the amendment and response to restriction requirement filed on November 1, 2002 (paper number 8). Accordingly, no additional amendment to the claim is required.

Priority Claim

At page 2 of the Office Action, the Examiner stated that "applicant has not acknowledged that the certified copies of the PCT/GB96/02770 and 9709900.6 have been received in this instant application or in any of the parent cases."

Applicants claim priority from the following applications: United States Application No. 09/079,400, filed May 15, 1998; United States Application No. 08/745,515, filed November 12, 1996; United Kingdom Application No. 9709900.6, filed May 15, 1997; United Kingdom Application No. 9601929.4, filed January 31, 1996; United Kingdom Application No. 9523019.0, filed November 9, 1995; and PCT Application No. PCT/GB96/02770, filed November 11, 1996. Specific reference in the specification to these prior applications was made by the preliminary amendment included with the filing of the present application.

Certified copies of United Kingdom Application No. 9709900.6 and PCT Application No. PCT/GB96/02770 have been filed in parent United States Application No. 09/079,400. Certified copies of the United Kingdom Applications Nos. 9601929.4 and 9523019.0 have been filed in parent application United States Application No. 08/745,515.

At pages 2-3 of the Office Action, the Examiner stated that claim 25 lacks support in certain of the priority applications of the present application. No claim 25 is pending in the present application. Furthermore, the claims currently pending in the present application are supported in prior applications having filing dates earlier than that of United States Application No. 09/079,400, filed May 15, 1998.

35 U.S.C. §103(a)

At pages 3-5 of the Office Action, the Examiner rejected claims 32-42 and 44-51 as allegedly unpatentable over Mathiowitz et al., WO 95/24929 ("Mathiowitz") taken with Yan et al. (1994) Journal of Controlled Release 32:231-241 ("Yan") and Yeh et al., WO 95/35097 ("Yeh").

In the present rejection, the Examiner cited on more than one occasion a passage from Mathiowitz (page 10) stating that "[t]he DNA, either in soluble form or dispersed as fine particles, is added to the polymer solution, and the mixture is suspended in an aqueous phase that contains a surface active agent such as poly(vinyl alcohol)." Following one such citation in the Office Action, the Examiner stated that "Mathiowitz *et al.* does not teach explicitly that the aqueous solution of DNA contains 1-40% of alcohol content." The Examiner also stated that: "Yan *et al.* teach that an further aqueous phase comprising 5% isopropanol is employed for the extraction"; and "Yeh *et al.* teach on page 30 that an aqueous solution of DNA containing 20% contents of ethanol (volume/volume) is effective for use in an emulsification technique to encapsulate DNA in a polymeric microparticle."

Independent claim 32 is directed to a composition containing a polymer microparticle and an aqueous solution of DNA containing a coding sequence, wherein the microparticle is 10μm or less in diameter, and wherein the aqueous solution of DNA has an alcohol content of 1 to 40% and is encapsulated inside the microparticle. Independent claim 43 similarly requires that the microparticles contained in the claimed composition contain an aqueous solution of DNA (containing a coding sequence) that has an alcohol content of 1 to 40%. The cited references

taken alone or in combination do not provide the requisite suggestion or motivation to construct the claimed compositions.

As stated in the Office Action, "Mathiowitz *et al.* does not teach explicitly that the aqueous solution of DNA contains 1-40% of alcohol content." Instead, Mathiowitz actually describes the use of polyvinyl alcohol (PVA) as a surfactant (i.e., a "surface active agent") that is added to a polymer solution containing DNA as part of a microparticle manufacturing process. Similarly, manufacturing methods described in the present application also describe the use of a surfactant (including PVA as an example) to prepare microparticles (see specification at, e.g., page 6, lines 7-24; page 9, lines 5-14; and page 19, line 13, to page 20, line 10). Used as a surfactant in the methods of Mathiowitz, PVA coats the *outside* surface of a microparticle. Nothing in Mathiowitz or any of the cited references suggests that PVA, when used as a surfactant in the process of manufacturing a microparticle, is deposited inside a microparticle such that the PVA is in an aqueous solution with DNA and is present at a concentration of 1-40% (as is required by the claimed compositions).

Neither Yan nor Yeh add what is lacking in Mathiowitz. Yan describes microparticle preparation methods that entail the preparation of an emulsion containing a protein, PLG, and methylene chloride. Similar to the methods disclosed by Mathiowitz, following vortexing or sonication, the resulting emulsion of Yan is added to a solution containing 1% PVA. As detailed above with respect to Mathiowitz, the PVA used by Yan acts as a surfactant and coats the *outside* surface of the microparticles. Following the mixing of the emulsion with PVA, Yan then describes the addition of an isopropanol solution to extract the methylene chloride. In such a method, isopropanol increases the solubility of methylene chloride and thereby facilitates its extraction. After stirring the isopropanol solution with the emulsion, isopropanol present in the mixture is then removed during centrifugation and three rounds of washing with water as detailed in Yan. Nothing in Yan suggests that isopropanol is deposited inside a microparticle such that it is in an aqueous solution with DNA at a concentration of 1-40% (as is required by the claimed compositions).

Yeh does not disclose or suggest that ethanol improves DNA encapsulation efficiency of an aqueous solution containing DNA, or that alcohol can be used in methods that feature the step of adding a (water-in-oil)-in-water double emulsion to a further aqueous solution to extract the organic phase. Without this latter step, Yeh's method would not produce microparticles akin to those of the claimed invention, which have an outer polymeric shell and an inner aqueous phase. Moreover, since Yeh does not suggest that alcohol can be used to increase DNA encapsulation efficiency, there would have been no reason to combine the disclosure of an alcohol-containing DNA solution in Yeh with the disclosure of Mathiowitz or Yan.

In light of these comments, applicants respectfully submit that Mathiowitz taken with Yan and Yeh would not have provided the skilled artisan, as of the filing date of the present application, with requisite suggestion or motivation to construct the claimed compositions. Accordingly, applicants respectfully request that the Examiner withdraw the rejection.

At page 6 of the Office Action, the Examiner rejected claims 32 and 40-43 as allegedly unpatentable over Mathiowitz taken with Yan, Yeh, and further in view of Estes, U.S. Patent No. 5,891,676 ("Estes"). According to the Examiner, "[t]o the extent that the combined cited references do not teach the use of a rotavirus VP1 polypeptide encoded nucleic acid as the immunogen encoded DNA in the delivery polymeric composition, Estes teaches that rotavirus VP1 polypeptide is an effective immunogen for use in DNA immunogenic composition."

As detailed above, Mathiowitz taken with Yan and/or Yeh does not suggest the compositions of any of claims 32-51. Estes, which is cited in the Office Action as a secondary reference describing rotavirus sequences, does not add what is lacking in Mathiowitz, Yan, and Yeh. In particular, nothing in Estes provides the requisite suggestion or motivation to construct a microparticle (as recited in the claims) that contains an aqueous solution of DNA that has an alcohol content of 1 to 40%. Accordingly, applicants respectfully request that the Examiner withdraw the rejection.

Obviousness-Type Double Patenting

At page 7 of the Office Action, the Examiner rejected claims 32-51 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-6 of commonly assigned U.S. Patent No. 6,270,795 ('795 patent) and further in view of Estes. Applicants respectfully traverse the rejection.

The '795 patent issued from an application (serial number 09/079,400, filed May 15, 1998) that is the parent of the present divisional application. During the course of prosecution of the parent application, the claims were subjected to a restriction requirement dated July 2, 1999. In response to that restriction requirement, applicants elected Group III, which corresponded to methods of encapsulating an aqueous solution of DNA in a polymeric composition, and canceled those claims directed to the non-elected inventions of Groups I and II. The non-elected invention of Group I (polymeric compositions containing a polymer microparticle and DNA) of the parent application is the subject matter of the present divisional application.

35 U.S.C. § 121 provides that

> [a] patent issuing on an application with respect to which a requirement for restriction under this section has been made, or on an application filed as a result of such a requirement, shall not be used as a reference either in the Patent and Trademark Office or in the courts against a divisional application or against the original application or any patent issued on either of them, if the divisional application is filed before the issuance of the patent on the other application.

Because the claimed invention of the present divisional application was subjected to a requirement for restriction by the Patent and Trademark Office in the parent application, the patent that issued from the parent application cannot now be used in an obviousness-type double patenting rejection against the present application. Accordingly, applicants respectfully request that the Examiner withdraw the rejection.

Conclusions

Enclosed is a Petition for Extension of Time and a check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney docket No. 12020-003002.

Respectfully submitted,

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Jack Brennan
Reg. No. 47,443

Fish & Richardson P.C.
45 Rockefeller Plaza, Suite 2800
New York, New York 10111
Telephone: (212) 765-5070
Facsimile: (212) 258-2291